REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Claim Status

Claims 1, 14-16, 21, 25, 39, 46, 67, 74 and 78 are currently amended. Claims 13, 38, 75, 80, 81 and 84 are cancelled herein. New claims 85-87 have been added. Support for the claim amendments, and new claims 85-87, may be found, for example, in the specification at paragraphs [0078], [0080], [0093]-[0096] and [0103] of U.S. Application Publication No. 2006/0153804, which corresponds to the present application, as well as in originally filed claims.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-7, 12, 14-32, 37, 39-46 and 67-74, 76-79, 82, 83 and 85-87 are now pending in this application.

II. Examiner Interview

Applicants wish to thank Examiner Kelly for an interview with Applicants' representative on January 28, 2010. Applicants will present their understanding from the interview as relevant to each rejection in the sections below.

III. Priority Application

The Examiner alleges that the priority application U.S. Appl. No. 60/414,097 fails to provide support for the claimed invention. Applicants respectfully disagree.

The specification of the priority document describes the particles as claimed, and appreciates their surprising stability. For example, the paragraph spanning pages 3-4 of the priority application states that the disclosed formulation optimizes stability of nucleic acid attached to inert metal carrier particles in the presence of a nucleic acid condensing agent and a metal ion chelating agent, "thereby promoting shelf-life of the particles and the quality of the nucleic acid delivered to target cells intact."

On page 18, lines 7-17, the priority application also describes the advantages of polyarginine, describing in particular short homopolymers of $(Arg)_x$, where x is from 2 to 10. For example, on page 18, lines 15-17, the priority documents states: "Typically, in a small peptide, x has a value from 2 to 10, for example, from 4 to 8. Homopolymers where x = 4 or 6, for example $(Arg)_4$ or $(Arg)_6$ are especially useful in the present invention." This passage, along with a previous sentence describing "a homopolymer of arginine $(Arg)_x$" (page 18, lines 7-8), clearly and expressly disclose a homopolymer of arginine of the formula $(Arg)_x$, wherein x is from 2 to 10.

Chelating agents recited in the pending claims are also described in the priority document, for example, beginning on page 19, line 19. Suitable sugars are described, for example, on page 20, lines 6-8. The priority application also describes the step of drying relevant particles, for example, on page 23, lines 22-26. Examples describe the physical stability of DNA on particles, and the impact of using poly-Arg peptides and recited sugars (such as sucrose or trehalose) and chelators (such as EDTA and DPTA), for example, on page 30, lines 17-20. Example 2, on page 32, also describes stability as tested at different temperatures, such as 4° C and 60° C.

At noted by the Examiner, the priority document does not present Example 4 and Table 2 exactly as disclosed in the pending application. As stated in Applicants' previous Reply and above, however, the priority document discloses the exact particles recited in the pending claims, as well as methods for making them. If one makes the exact particles recited in pending independent claims (as disclosed in the priority document), one necessarily makes dried particles

having a half life of at least 27 days at 40° C (i.e., having enhanced stability, as described in the priority document). Because the enhanced stability is inherent in the recited particular particles, it is not relevant that the priority document does not disclose Table 2 in the instant application. Page 30, lines 17-20, of the priority document, for example, presents results indicating enhanced stability when using EDTA and/or sucrose or trehalose with the poly-Arg peptide, as compared to other chelators or sugars. Thus, Applicants both possessed and disclosed particles recited in the present pending claims. Contrary to the Examiner's assertion, the fact that such stability was surprising does not negate the fact that Applicants possessed and disclosed the particles.

Thus, Applicants submit that the priority application, by disclosing the formulation and the increased stability of the claimed particles, supports the present claims.

IV. Claim Rejections under 35 U.S.C. § 112

(i) Indefiniteness

Claims 1-7, 12-32, 37-46 and 67-83 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Office Action at 4. Applicants respectfully traverse this rejection.

During the in-person interview with Applicants' representative on January 28, 2010, the Examiner clarified his position that the claims as written allegedly do not describe the parameters by which stability is measured, and therefore, according to the Examiner, cover situations where any recited particles, no matter the surrounding or solution, would be stable for a certain number of days at 40° C. Applicants' representative explained that the stability studies were performed on dried powder of the particles, as shown in Examples 2-4 in the specification. The Examiner indicated that if Applicants recited "dried" or some variation thereof in the claims regarding the recited particles, Applicants would overcome this rejection.

Solely in an effort to advance prosecution, and not acquiescing in the propriety of the rejection, claims 1, 25 and 67 and new independent claim 85, from which the remaining rejected claims depend, now recite that the particles are dried to a powder.

One of skill in the art would have easily understood the meaning of the claim phrase in question, as it applies to the presently claimed dried particles. Examples 1 and 2 provide ample guidance on how to make the particles, as well as how to measure the half life of the nucleic acid contained on the dried particles, such as by gel electrophoresis or HPLC methods. As such, a skilled artisan would have had no difficulty in ascertaining whether particles infringed Applicants' claims or not and would therefore readily recognize the metes and bounds of the claims.

Applicants respectfully disagree with the Examiner's position in the Office Action that conditions, such as pressure, exposures to extraneous components such as acids, bases and enzymes, or length of the DNA, must be defined for one to understand what the phrase "wherein the particles suitable for delivery have a half life of at least 27 days at 40° C" means in the claims. Acceptability of claim language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. *See, e.g.,* M.P.E.P. § 2173.05(b). Independent claims recite elements required to make the inventive particles. The term "half life" is well known in the art as discussed in the previous Reply filed August 7, 2009. Thus, one of skill in the art, upon reading the specification, would have been able to make the inventive dried particles, as well as identify particles that fall within the scope of the claims, regardless of additional unrecited components mentioned by the Examiner.

In the Office Action, the Examiner also asserts that there are two possible interpretations for claims 1, 25 and 67. Specifically, the Examiner states that "either a composition is claimed in which particles have a specific half-life, or, under an alternative interpretation, appears to claim only those particles which are suitable for delivery and are at least half-active after 20 [*sic*-27] days at 40.deg.C." Office Action at 5. Applicants respectfully disagree and point out that

independent claims 1 and 67 are directed to "[p]articles suitable for delivery....wherein the dried particles have a half life of at least 27 days at 40° C." Thus, the claims are clear on their face. It is not the case that "alternative, non-coextensive interpretations" of the recited claims exist, as alleged by the Examiner.

Finally, the Examiner contends that claim 1 is not clear because it recites that particles are "obtainable" by the process recited in the claim, "but fails to provide the structure of the particles obtained." *Id.* Applicants respectfully disagree. Solely in an effort to advance prosecution, and not acquiescing in the propriety of the rejection, however, Applicants have amended claim 1 to recite that "the particles are obtained by a method comprising the steps of...."

Because the pending claims have clear metes and bounds, Applicants respectfully request that the rejection be withdrawn.

(ii) New matter

Claims 1-7, 12-32, 37-46 and 67-84 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement for comprising new matter. Office Action at 7. Applicant respectfully traverses this rejection. Specifically, the Examiner objects to the phrase "wherein the particles suitable for delivery have a half life of greater than at least 27 days at 40° C."

As stated in M.P.E.P. § 2163.07, "[a]mendments to an application which are supported in the original description are NOT new matter." Applicant respectfully asserts that the present amendment is supported in the as-filed specification.

The Examiner maintains that "there are compositions that Applicant has demonstrated have less stability under the conditions, e.g. TABLE 2, and fall within the claims; there is no explicit recitation to those embodiments which meet the claimed limitation of stability...." Office Action at 10. Applicants maintain that the point raised by the Examiner is irrelevant to a new matter rejection. As stated above, new matter concerns amendments to an application that

are not supported in the as-filed specification. As discussed below, and in previously Replies, the claimed subject matter is supported by the specification as filed. Even assuming the application discloses embodiments that fall outside the scope of the claims (e.g., particles having a half life less than 27 days at 40 °C), that disclosure does not raise a new matter consideration when the application clearly discloses the claimed invention (i.e., particles having a half life of at least 27 days at 40 °C).

In addition, the Examiner comments that "Applicant argues that the single inoperative embodiment of Table 2 does not render the claims unpatentable for enablement.... Such is not persuasive. This has nothing to do with enablement." Office Action at 11. Indeed, Applicants' point is that "inoperable" embodiments, which the Examiner alleges fall within the scope of the claims, are irrelevant to a new matter rejection. In any event, the point is now moot because the specific "inoperable embodiment" concerning the Examiner does not fall within the scope of the claims as amended herein.

During the January 28, 2010 interview, when discussing the new matter rejection, the Examiner emphasized that one formula in Table 2 in Example 4, i.e., particles made in trehalose and DTPA ("TA101.4" formula), presented a half life (16 days) less than that with spermidine/$CaCl_2$ (19 days) and less than "at least 27 days" as recited in the claims.

Solely in an effort to advance prosecution, and not acquiescing in the propriety of the rejection, amended claims 1, 25 and 67 and new independent claim 85, now recite that either the metal ion chelating agent is EDTA, or a sugar comprises sucrose, or both. Thus, "TA101.4" formula particles now fall outside the scope of the pending claims as amended. Regarding the recited claims, Table 2 clearly indicates that such particles, obtained in the presence of EDTA, sucrose or both, had a half life of 27 days or greater. Specifically, at 40°C, formula "TA101.2" (DNA + TetraArg + DTPA + sucrose) had a half life of 27 days, formula "TA101.1" (DNA + TetraArg + EDTA + sucrose) had a half life of 65 days, and formula "TA101.3" (DNA + TetraArg + EDTA + trehalose) had a half life of 59 days.

During the interview, the Examiner also emphasized his opinion that Applicants did not understand, i.e., "have possession of", their invention until after Applicants added the claim amendment relating to the "half life of at least 27 days." As explained by Applicants' representative in the interview, Table 2 clearly discloses that the inventors possessed the invention at the time of filing, even if they did not specifically recite the "half life of at least 27 days" element in claims until later in prosecution. During the interview, the Examiner suggested that Applicants provide a sworn statement by an expert stating that those skilled in the art, reading the specification as filed and relevant prior art, would have thought Applicants were in possession of the invention as claimed at the time of filing.

Again, solely to advance prosecution, Applicants submit herewith the Declaration of Dr. Phil White Under 37 C.F.R. § 1.132 ("Declaration"). In the Declaration, Dr. White opines on the data in Table 2 of the present application. In particular, it is Dr. White's opinion that "data disclosed in Table 2 of the '010 application expressly described DNA coated-particles produced using formulations containing an arginine homopolymer, a metal chelating agent and a sugar." Declaration at ¶ 9. Dr. White continues, stating that the data in Table 2 expressly describes particles "such as those obtained in the presence of, *inter alia*, EDTA and/or sucrose, had a half-life of 27 days or greater, i.e., 'at least 27 days'." *Id.*

In view of the information present in the specification, Dr. White concludes that "a knowledgeable person, informed by the data presented in Table 2, would have understood that the inventors of the '010 application realized that they had prepared relevant particles having a half-life of at least 27 days at 40°C." *Id.* at ¶ 10. As such, in Dr. White's opinion, Applicants were in possession of the invention at the time of filing. *Id.* at ¶ 11.

Because the instant specification provides ample and literal guidance for the claimed invention, the claims cannot comprise new matter. Therefore, in view of the statements above and the Declaration of Dr. White, Applicants respectfully request that the rejection be withdrawn.

V. Claim Rejections under 35 U.S.C. § 103

(i) Sanford, Balhorn, Oard

Claims 1-5, 7, 12-13, 17-20, 22-30, 32, 37, 38, 42-45, 67, 73 and 84 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,204,253 ("Sanford") and Balhorn (*Mol. Reprod. Dev.*, (2000) 56: 230-34) ("Balhorn"), as evidenced by Oard (*Plant Cell. Tiss. and Org. Cult.*, (1993) 33(3): 247-50) ("Oard"). Applicants respectfully traverse this rejection. Despite the Examiner's allegation, one of skill in the art would not have substituted the arginine-rich peptides described in Balhorn for the spermidine disclosed in Sanford (or Oard) for use in making the claimed particles. Those skilled in the art would had no reason to combine Sanford and/or Oard with Balhorn.

As discussed previously, the art cited by the Examiner does not arrive at the claimed invention. Sanford discloses the ballistic delivery of tungsten particles, onto which plasmid DNA is condensed in a buffer containing EDTA in the presence of spermidine/calcium chloride. (*see* col. 15, lines 14-32). Therefore, Sanford teaches the use of spermidine (a polyamine that has distinctly different chemical and structural properties from the homopolymers of polyargine used in the present invention) with calcium chloride for DNA condensation onto particles. Furthermore, Sanford fails to address stability of its disclosed particles altogether.

Like Sanford, Oard teaches the use of spermidine $CaCl_2$ to condense DNA onto a microparticle and is therefore duplicative of the Sanford reference. *See* Oard at 249, 1st col., bottom paragraph. Oard, like Sanford, completely fails to suggest the use of a homopolymer of arginine for this process, but rather states that prior to DNA precipitation, one can rinse microcarriers with poly-L-lysine. *Id.* at 1st col., second from bottom paragraph. In this context, Oard states "[t]he use of gold flakes and poly-L-lysine did reduce clumping relative to the tungsten particles, but did not eliminate the problem entirely." *Id.* at 2nd col., 1st paragraph (emphasis added). Additionally, like Sanford, Oard does not address stability issues because the

disclosed "microcarriers" were prepared and used "as soon as possible after precipitation because the amount of clumping increased over time." *Id.* at 2nd col., 1st paragraph.

In the Office Action, the Examiner asserts that one of skill in the art would have been motivated to substitute the arginine rich peptides of Balhorn for the spermidine component of Sanford. During the January 28, 2010 interview, the Examiner clarified his position in this regard. As Applicants understand it, the Examiner's position is that one would have been motivated to use an arginine peptide of Balhorn in place of the spermidine in Sanford because the arginine peptide would be beneficial when using the particles later, i.e., would help promote the dissociation, and therefore expression, of the DNA once injected into a cell. According to the Examiner, because having it in a solution would be helpful when using the particle after it is made, one would have been motivated to use arginine peptides when making the particle also.

As discussed above, solely in an effort to advance prosecution, and not acquiescing in the propriety of the rejection, amended claims 1, 25 and 67, and new claim 85, now recite "drying the particles" and "dried particles." As suggested by the Examiner in a subsequent telephonic interview on January 28, 2010 (immediately after the in-person interview), those skilled in the art, in light of cited references and especially Balhorn, would not have been motivated to make dried particles as recited in the pending claims.

Balhorn discusses arginine homopolymers as they relate to the decondensation of a DNA-protamine complex, not the long term stability of a dried metal carrier particle coated with a nucleic acid. Indeed, Balhorn shows dissociation of DNA from an arginine-rich peptide in solution. *See, e.g.*, Balhorn at 232 ("The rate of dissociation of the protein or peptide could then be determined by moving the same condensed DNA back across the interface into the buffer containing only DNA."). Thus, as the Examiner acknowledges, the dissociation of the DNA from the protamine complex is observed in solution. Office Action at 15-16 ("In this case, the particle precipitated compositions do not release with the kinetics of Balhorn, until it is solvated in solution.).

Consequently, one of skill in the art would not have relied upon the teachings of Balhorn, which draw conclusions regarding DNA decondensation with an arginine peptide based solely on experiments performed in solution, to design a stable dried particle coated with DNA. One of skill in the art would not have considered Balhorn when making such particles, because what occurred when using particles in solution (i.e., DNA dissociation from the particles once inside the cell) would be irrelevant to methods of making stable dried particles (i.e., where keeping DNA condensed on the particles would be the goal during storage).

In fact, as previously explained in the prior Reply, if those skilled in the art considered Balhorn at all, they would have understood that this reference taught away from the claimed invention by suggesting that polyArg stimulated DNA dissociation from the particles, i.e., instability of DNA on the particle.

Alternatively, one would not have considered Balhorn at all in the context of making stable dried particles having DNA condensed on their surface. In fact, in the Office Action, the Examiner himself asserts that dissociation in solution is irrelevant to the stability of DNA on a dried particle:

> [T]he dissociation in solution is irrelevant, when precipitated onto the particle....[T]he stability of the precipitate does not revolve on the dissociation of the polyArg, or spermidine, because it is precipitated. To wit, in the precipitated phase, the Arginine concentration is necessarily much higher, due to the exclusion of water, and hence, the off rate in solution is no longer applicable....

Office Action at 17. In other words, the fact that polyArg increased DNA dissociation from particles in solution would not have provided a reason to those skilled in the art to use a homopolymer of arginine when making stable dried particles having DNA condensed onto the surface.

In the Office Action, the Examiner does not find persuasive the teaching of Adami, a reference previously cited by Applicants, to demonstrate that it was unexpected for shorter

polymers of arginine to provide increased stability. Office Action at 19. The Examiner dismisses Adami because "Adami's stability is drawn to solution forms of peptide/DNA condensates, not condensates which are precipitated onto a microparticle." *Id.* (emphasis added). In other words, the Examiner again underscores his understanding that prior art discussing what happens to particles in solution is not applicable to the present invention. For the same reasoning, Applicants assert that the Examiner cannot rely upon Balhorn, at minimum because the presently claimed particles are dried, i.e., not in solution.

Applicants assert that for the reasons provided above, and for the reason provided by the Examiner, Balhorn is irrelevant to the presently claimed particles. One of skill in the art would have had no reason to combine the teachings of Balhorn with Sanford to produce stable dried particle suitable for ballistic delivery containing DNA.

Finally, Applicants submit that the stability of the recited particles was a surprising and unexpected result. Nothing in Sanford or Oard suggested such stability (or even addressed or measured stability) or otherwise indicated specific reagents or methods needed to obtained particles having the recited stability. Nothing in Sanford or Oard suggested the use of a homopolymer of arginine at all, much less the use of a homopolymer of arginine in combination with EDTA, sucrose or both, to make stable dried particles. Likewise, nothing in Belhorn (either alone, or in combination with Sanford and/or Oard) suggested making dried particles at all, or what one might need to make dried particles having the recited stability. As an aside, Applicants note that the Examiner opines that "Applicant's 'surprising result' is even drawn to abnormal conditions. 40 deg C is simply not a standard condition in which these compositions are stored." Office Action at 14. In response, Applicants point out that the pending claims do not require that one store particles at 40° C. The claims simply reflect that claimed particles exhibit surprising stability, i.e., they are stable for a significant time even 40° C, thereby indicating such particles are even more stable, e.g., stable for even longer periods of time, at room temperature.

Thus, for at least the foregoing reasons, those skilled in the art would not have considered Applicants' claimed particles, or methods for making them, obvious. Accordingly, Applicants submit that the rejection should be withdrawn.

(ii) Sanford, Balhorn, Oard, Cherng and Kwok

Claims 1-5, 7, 12-15, 17-30, 32, 37-40, 42-46, 67 73, 79, 80, 82, 83 and 84 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sanford and Balhorn, as evidenced by Oard, and further in view of Cherng *et al.* (*Pharm. Res.*, 16(9): 1417-23 (1999) ("Cherng") and Kwok *et al.* (*Intl. J. of Pharma.* 203:81-88 (2000) ("Kwok"). Applicants respectfully traverse this rejection.

The deficiencies of Sanford, Balhorn and Oard are addressed in detail above and remain applicable for the present rejection. Specifically, one skilled in the art would not have considered substituting arginine-rich peptides used in the aqueous experiments of Balhorn for spermidine when making the dried particles as presently claimed. Cherng does not overcome these deficiencies, as at best, it teaches the use of sucrose in polymer-plasmid complexes.

Applicants reiterate that Cherng does not precipitate DNA onto metal particles. Instead, Cherng is directed solely to the stability of plasmid-polymer based complexes ("polyplexes") in aqueous dispersion and as a lyophilized preparation. The polymer used in the polyplexes of Cherng is a methacrylate-based polymer, which is chemically very dissimilar to short homopolymers of arginine and inert metal particles. Cherng carefully notes that the results are only applicable to the polyplexes described therein, and at best, might extend to other polyplexes and lipid formulations (page 1423, second paragraph). There is no mention in Cherng of inert metal particles.

The Examiner attempts to rebuts Applicants' statement by arguing that Cherng comments that the results "might be extended to other polyplex and lipoplex formulations." Office Action at 23 (emphasis added). The Examiner's argument, however, completely ignores that Cherng

explicitly cautioned from applying the conclusions made therein to other systems. In the face of this explicit cautioning by the authors, one of skill in the art are would not have had any reason to adapt the teachings of Cherng to other systems.

The Examiner then cites Kwok for an additional reference in support of the use of sucrose as an excipient to stabilize DNA condensates. Office Action 22. It is unclear what support Kwok adds to the Examiner's rejection above Cherng. Kwok teaches the use of sucrose as a lyoprotectant for freeze-dried DNA/poly-lysine condensates. *See* Kwok at Abstract and page 86, left column, last paragraph. Again, Kwok does not relate to the precipitation of DNA onto particles in the presence of a metal chelator and a homopolymer of arginine and provides no evidence or insight into whether sucrose might help enhance stability of the DNA on such dried particles at 40° C or room temperature.

Finally, Cherng and Kwok do not provide any disclosure that would overcome the previously discussed failure of the cited combination of references to teach or suggest the presently claimed particles. The effect of short homopolymers of arginine and a chelator on dried particle stability is not discussed in this reference or the others. Therefore, Applicants respectfully request that the rejection be withdrawn.

(iii) Sanford, Balhorn, Oard, Cherng, Barman, Livesey

Claims 1-7, 12-32, 37-46, 67-73, 76, 79, 80, 82, 83 and 84 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sanford and Balhorn, and in view of Oard, Cherng, and Kwok, and further in view of U.S. Publication No. 2004/0142475 ("Barman"), as further evidenced by U.S. Patent No. 6,194,136 ("Livesey"). Applicants respectfully traverse this rejection.

The deficiencies of Sanford, Balhorn, Oard, Cherng and Kwok are addressed in detail above and remain applicable for the present rejection. Specifically, one of skill in the art would not have been motivated to use the arginine peptides of Balhorn or the sucrose lyoprotectant of

Cherng and Kwok in the ballistic delivery methods of Sanford or Oard. Barman and Livesey do not overcome these deficiencies.

Barman is cited by the Examiner as allegedly teaching that saccharides may be used to stabilize nucleic acid protein complexes, and that HPV, HIV, HBV and HSV antigens may be encoded as transgenes for the expression of antigens. Similarly, Livesey is cited as allegedly demonstrating that sugars, including raffinose, can be used as stabilizers. As discussed in Applicant's previous response, however, neither of these references overcome the defect of the other references, which is the failure to teach or suggest the presently claimed dried particles. Barman teaches the use of polymeric microparticles, not inert metal particles, and mentions that stabilizers may be used, with examples including sugars and cationic peptides. *See* paragraphs 41 and 46. Barman neither discloses nor suggests the use of short homopolymers of arginine and a chelator, nor their effect on stability of the particles. Likewise, Livesey provides only general disclosure of cryopreservatives, and does not mention inert metal particles, short homopolymers of arginine or chelators. Thus, the addition of these two references to the other references fails to disclose surprising characteristics of the present invention.

The Examiner is now picking and choosing from six different references in an attempt to arrive at Applicants' invention. The Examiner's asserted reasons for combining all of these references amount to hindsight reconstruction, and not the reasoning of one of ordinary skill in the art. As such, Applicants respectfully request that the rejection be withdrawn.

(iv) Sanford, Balhorn, Oard, Cherng, Barman, Livesey and various

Claims 1-7, 12-32, 37-46 and 67-83 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sanford and Balhorn, as evidenced by Oard, Cherng, Kwok, Barman, and Livesey and further in view of the knowledge of the artisan as evidenced by (i) Ramos et al. (1997) Applied and Environmental Microbiology (e.g., ABSTRACT); (ii) Ericksson et al. (2003) Pharmaceutical Research, 20(9): 1437-43 (e.g., ABSTRACT); (iii) Kaushik et al. (2003) Journal of Biological Chemistry, 278(29): 26485-65 (e.g., ABSTRACT); (iv) Garg et al. (2002)

Proceedings of the National Academy of Science, USA, 99(25): 15898-903 (e.g., ABSTRACT); (v) More et al. (1998) Hindustan Antibiotics Bulletin, 40(1-4): 1-4 (ABSTRACT ONLY); (vi) Joshi et al. (2001) AAPS PharmSciTech., 2(4): 25 (ABSTRACT ONLY), (vii) Ruan et al. (2003) European Journal of Biochemistry, 270: 1654-61 (e.g., ABSTRACT), and (viii) Schellman (2003) Biophysical Journal, 85(1): 108-25. Applicant respectfully traverses this rejection.

The deficiencies of previously cited references are addressed in detail above and remain applicable for the present rejection. Specifically, one of skill in the art would not have used the arginine-rich peptides of Balhorn in the ballistic delivery methods of Sanford or Oard in combination with the sucrose or saccharides of Cherng, Barmen or Livesey. The remaining references do not overcome this limitation.

The Examiner adds a lengthy list of various references as allegedly teaching the use of trehalose in the present invention. As discussed above, however, these references are not directed to any technology similar to the claimed particles, much less those having the surprising characteristics of the present invention. Mere recitation of many references do not make up for the fact that none overcome the deficiencies of the main references as previously discussed. These references are merely drawn to various protein solutions and cryopreservation, not particles suitable for delivery from a particle-mediated delivery device. Thus, the addition of these references to the other references still fails to disclose or suggest the present invention. Applicants respectfully request that the rejection be withdrawn.

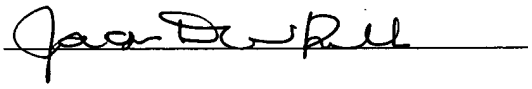
Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date: March 22, 2010

By 

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